

Safety of thrombolytic treatment in patients with central venous cannulation

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Abstract

Objectives—To determine the safety of thrombolytic treatment in patients with central venous cannulation.

Background—Thrombolytic treatment significantly reduces mortality in patients with myocardial infarction. Because of the fibrinolytic state induced and the potential for haemorrhagic complications, thrombolysis is currently considered a strong relative contraindication in patients who have had central venous cannulation. There are few data available to support this practice.

Methods—Complications in 56 consecutive patients admitted between 1989 and 1992 with infarction and who had cannulation shortly before, or within 24 h of thrombolysis were studied.

Results—Central venous access was achieved via the subclavian route in 52 patients, the internal jugular in three, and the supraclavicular in one. The main indications were for inotropic drugs in 15 patients, pacing in 17, amiodarone infusion in 19, and pressure monitoring in five. Minor haemorrhagic complications occurred in five patients. Two of these patients required either blood or plasma transfusion. Possible major haemorrhagic complications occurred in one patient who became hypotensive shortly after cannulation. Two further patients with severe cardiac failure became hypotensive after cannulation but there was no radiological evidence of effusion and the hypotension was attributed to worsening cardiac failure. Importantly, none of the 19 patients who had cannulas for amiodarone infusion developed significant bleeding complications.

Conclusion—Central cannulation in the fibrinolytic state is associated with a low incidence of important bleeding complications. Thrombolysis should not be withheld in these patients. Cannulation via the subclavian route, however, should be avoided in patients undergoing thrombolysis.

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Keywords: myocardial infarction; thrombolytic treatment; central venous cannulation

Acute myocardial infarction is associated with a significant mortality. Major trials in recent

years have shown a reduction in infarct size¹ and mortality when these patients are treated with a thrombolytic agent.²⁻⁵ Thrombolysis, however, induces a generalised fibrinolytic state which can lead to haemorrhagic complications. For this reason, thrombolytic treatment is considered to be a strong relative or even an absolute contraindication in patients who have had central venous cannulation.^{6,7} At present, few data are available to support the practice of withholding thrombolytic treatment and to document haemorrhagic complications associated with central venous cannulation.

Central venous cannulation is frequently employed in the management of patients with acute myocardial infarction. Moreover, a significant number of myocardial reinfarctions requiring a repeated dose of thrombolytic agent occur in the first few days after the initial infarction.⁸ Some of these patients would have had recent central venous cannulation and be denied thrombolysis because of a perceived risk of severe bleeding. We studied a consecutive series of patients who had central venous cannulation shortly before or after thrombolytic treatment to determine the safety of thrombolysis in association with central venous cannulation.

Patients and methods

PATIENTS

All patients admitted to the coronary care unit at York District Hospital between 1989 and 1992 who underwent central line insertion shortly before or within 24 h of thrombolytic treatment were included in the study. The study comprised 56 patients of whom 35 were male and 21 female patients. Their mean (SD) age was 67 (9) years. The mean (SD) (range) age of the men was 66 (9) (44-82) years and of the women 68 (8) (50-81) years.

The patients were divided into four groups corresponding to the main indication for central venous cannulation: inotropic drugs, amiodarone, temporary transvenous cardiac pacing, and pressure monitoring. All venous cannulations were performed by either a senior house officer or registrar, qualified for between two and five years. Table 1 summarises the number of patients in each group and their characteristics.

METHODS

Case notes of all patients included in the study were reviewed by two observers for possible complications secondary to central

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Table 1 Patients characteristics

	Amiodarone	Pacing	Inotropes*	Pressure monitoring
No of patients	19	17	15	5
Sex (M/F)	16/3	8/9	9/6	2/3
Mean (SD) age (years)	66(9)	68 (10)	66 (9)	65 (7)
Myocardial infarction				
Anterior	9	2	4	1
Inferior	9	14	9	4
Others	1†	1‡	2§¶	0
Previous myocardial infarction	7	2	8	2

Values are number of patients unless otherwise stated.

*Dobutamine and dopamine, †Left bundle branch block.

‡Anterior and inferior myocardial infarction. §Electrocardiogram showing ST segment depression without elevation.

¶Patient paced, unpaced electrocardiogram not available.

venous cannulation. In particular we looked for documented external bleeding or haematoma, haemothorax (on post-procedure chest x ray), low or decreasing central venous pressure, decreasing serum haemoglobin, unexplained hypotension, and death.

Minor haemorrhagic complications are defined as non-life threatening complications resulting from blood loss associated with venous cannulation. These were easily managed conservatively or with blood transfusion. The haemodynamics of the patients were not compromised. Major haemorrhagic complications are defined as significant blood loss resulting in severe hypotension (systolic blood pressure ≤ 90 mm Hg) and tachycardia with decreasing central venous pressure. These would be regarded as potentially life threatening.

Table 2 Patients with heart failure and the thrombolytic, anticoagulation, and antiplatelet regimens used in each group of patients

	Amiodarone	Pacing	Inotropes*	Pressure monitoring
Congestive cardiac failure before central venous cannulation	8	2	15	5
Severe hypotension (Systolic blood pressure ≤ 90 mm Hg)	3	1	13	5
Thrombolytic agent				
Streptokinase	18	15	14	4
Tissue plasminogen activator	1	2	1	1
Heparin (full dose)	2	2	2	1
Warfarin	0	0	0	0
Aspirin	15	13	12	4

Values are number of patients. *Dobutamine and dopamine.

Table 3 Characteristics of central venous cannulation

	Amiodarone	Pacing	Inotropes	Pressure monitoring	Difficulty associated with central venous cannulation*
Central venous cannulation route:					
Subclavian	17	16	14	5	8†
Internal jugular	2	1	0	0	1
Supraclavicular	0	0	1	0	0
Device:					
Desivalve	5	17	4	4	4
Triple	12	0	11	1	5
Other	2‡	0	0	0	0
Central venous cannulation* difficult	3	3	3	0	

*Documented in the case notes. † = Unable to cannulate the right subclavian vein in two patients (left subclavian vein cannulated instead). Right subclavian arterial puncture in one patient (antecubital vein cannulated instead). ‡One patient had a Wallace device and the other a Leadercath device.

The χ^2 test with Yates' correction was used to calculate the difference between two groups of patients.

Results

PATIENTS

Blood pressure was monitored at 15 min intervals after central venous cannulation where possible. These data were considered adequate in all patients. Congestive cardiac failure was present in 30 patients before central venous cannulation (table 2). The incidence of congestive cardiac failure and severe hypotension (systolic blood pressure ≤ 90 mm Hg) was higher in patients cannulated for inotropic treatment and pressure monitoring than in those cannulated for amiodarone infusion or cardiac pacing.

THROMBOLYTIC, ANTICOAGULATION AND ANTIPLATELET TREATMENT

Fifty one (91%) of the 56 patients received streptokinase for the treatment of acute myocardial infarction with five patients receiving tissue plasminogen activator (table 2). There were no significant differences between the number of patients receiving streptokinase in each of the patient groups ($P > 0.05$ in each case). Seven patients received full dose heparin. Five as routine adjunct with tissue plasminogen activator and two with streptokinase as part of the GUSTO trial.⁹ All other patients received subcutaneous heparin 5000 U twice daily. No patients were taking concomitant warfarin treatment. Aspirin was given to 44 (79%) of the 56 patients, with no significant difference between each group of patients ($P > 0.05$ in each case).

CENTRAL VENOUS CANNULATION

Table 3 summarises the routes of venous approach and the type of catheter used in each group of patients. Central venous access was obtained via the subclavian route in 52 patients, the internal jugular in three and the supraclavicular route in one. A single lumen catheter with haemostatic valve (Desivalve, Vygons, Cirencester) was used in 30 patients, a triple lumen catheter in 24, a "Wallace" single lumen catheter over needle device in one, and a "Leadercath" conventional single lumen catheter in one. Central venous cannulation was documented in the case notes of nine patients as being difficult.

One patient was cannalised for amiodarone infusion 15 min after the start of streptokinase. It was discovered 9.5 h later that the line was arterial. This was confirmed with blood gas measurement. The line was withdrawn and a drum catheter inserted via the antecubital vein. Central venous pressure measurement was stable and chest x ray showed no evidence of haemothorax. Recovery was otherwise uncomplicated.

COMPLICATIONS

Central venous pressure was serially monitored and the data were judged complete in 20 (36%) of the 56 patients (table 4). Fifteen

Table 4 Complications and mortality of patients who received central venous cannulation

	Amiodarone	Pacing	Inotropes*	Pressure monitoring
Complications:				
Major	0	1	0	0
Minor	2	2	1	0
Central venous pressure:				
Measured	2	3	10	5
Low central venous pressure	0	0	0	0
Chest x ray:				
Performed	13	12	11	1
Effusion	0	1	1	0
No of deaths at:				
3 days	1	1	9	3
7 days	4	1	11	3

Values are number of patients. *Dobutamine and dopamine.

(75%) of these patients were in the inotropic and pressure monitoring groups. No patient had a low or decreasing central venous pressure.

A chest x ray was performed after central venous cannulation in 37 patients. The x ray of two patients showed blunting of the costophrenic angle suggestive of a small pleural effusion. Both chest x rays also showed evidence of pulmonary venous congestion with upper lobe diversion.

HAEMORRHAGIC COMPLICATIONS

Serial haemoglobin measurement was performed when clinically indicated. Minor bleeding complications occurred in five patients, all of whom had suffered inferior myocardial infarction. Table 5 summarises their characteristics.

Major complications, possibly attributable to central venepuncture, were sustained by a 70 year old woman (patient A) with an acute anterolateral myocardial infarction treated with streptokinase and aspirin. The patient had a history of myocardial infarction 6 years previously. She developed cardiac failure with increased jugular venous pressure, hypotension (blood pressure 80/60 mm Hg), and low urine output. Right subclavian venous access was obtained with difficulty for dobutamine and dopamine infusion (7.45 h after initiation of streptokinase). At 1 h post-procedure, her blood pressure suddenly

became unrecordable and her heart rate increased to 130 beats/min. Her dobutamine dose was increased and a peak systolic pressure of 90 mm Hg was achieved. She died of continuing cardiac failure, however, 25.5 h after venous cannulation. No post-procedural chest x ray was performed and central venous pressure was not monitored as her jugular venous pressure was persistently raised.

Two further patients developed hypotension after venous cannulation. A 65 year old man (patient B) with a history of three previous myocardial infarctions suffered a further antero-septal infarction and was treated with streptokinase. He was receiving long-term dipyridamole treatment. A subclavian venous line was inserted (8.25 h after starting streptokinase) for amiodarone, dobutamine, and dopamine infusion after cardiac arrest with ventricular fibrillation and severe pulmonary oedema post-arrest. His blood pressure decreased from a post-arrest measurement of 110/60 mm Hg to 50/35 mm Hg after venous cannulation. He died 90 min after cannulation. A 73 year old man (patient C) treated with streptokinase for inferior infarction developed complete heart block requiring temporary pacing. This was attempted without success from the right subclavian approach (3 h after starting streptokinase) and was inserted through the left subclavian vein. The patient had continuous bleeding and a large bruise on the right puncture site. He became hypotensive (blood pressure decreased from 100/60 mm Hg to 55/40 mm Hg) with loss of consciousness 4 h after venous cannulation. He died 16.5 h after the procedure. Both patients had a post-procedural chest x ray with no evidence of effusion. Cardiac failure was the likely cause of hypotension.

MORTALITY

Fourteen patients (25%) died within three days of admission. Twelve (86%) of these patients were in the inotropic or pressure monitoring groups. Mortality in these two groups was significantly higher than in the amiodarone ($\chi^2 = 10.8$, $P < 0.01$) and pacing groups ($\chi^2 = 9.55$, $P < 0.01$) in which one patient of each group died. Three further patients in the amiodarone and two in the inotropic group died of worsening cardiac failure by day 7.

Discussion

Central venous cannulation to facilitate drug administration, pressure monitoring, or temporary transvenous pacing is not uncommon in the setting of acute myocardial infarction. It does, however, present the clinician with an additional potential hazard to consider when weighing up the relative risks and benefits of thrombolytic treatment in a patient with infarction and a central line already inserted. Some authorities regard even one unsuccessful attempt at central line placement as an important contraindication to thrombolysis.^{6,7} There are, however, few data available to

Table 5 Minor haemorrhagic complications

Patient	Sex	Age (years)	Aspirin	Complications	Management
1*	F	81	Yes	Prolonged bleeding from puncture site	Two units of fresh frozen plasma
2*	F	55	Yes	Haemoglobin dropped from 11.2 to 9.3 dg/l in 4 days	Two units of blood
3	M	78	Yes	Moderate haematoma	None
4	M	60	No	Moderate bleeding from puncture site	Pressure dressing
5	M	47	Yes	Bleeding from puncture site	Pressure dressing

No other cause of anaemia was noted.

support this practice. The results of this study suggest that central venous cannulation is associated with a low incidence of significant bleeding complications in the presence of thrombolysis.

We included only patients who received central venous cannulation within 24 h of thrombolytic treatment because fibrinogen levels are known to be reduced and patients are at increased risk of haemorrhage during that time interval.^{10,11}

Major haemorrhagic complications directly attributable to central venepuncture possibly occurred in one patient. Even then patient A was already in significant cardiac failure before venous cannulation and cardiogenic shock was equally likely to have been the cause of hypotension. Unfortunately, this patient did not have a post-cannulation chest x ray and a haemothorax could not be confidently excluded. Patients B and C were in significant cardiac failure before central venous cannulation. The cause of hypotension was likely to be cardiac failure as significant bleeding would have been demonstrated in the post-cannulation chest x ray.

Most patients with congestive cardiac failure and significant hypotension were in the inotropic group. The mortality in these patients would be expected to be high. This is the case in our patients with a three day mortality of 60%. We chose to examine three day mortality because haemorrhagic complications are unlikely to be the main cause of death after this time. The seven day mortality is also listed in table 4 for comparison. Importantly, only one (5%) of the 19 patients in the amiodarone group and one (6%) in the pacing group died within three days. The patient receiving amiodarone who died was canalised via the internal jugular venous route during cardiac arrest. The patient was in ventricular fibrillation and despite amiodarone resuscitation failed. The patient in the pacing group who died has already been described (patient C).

Only one patient in this series sustained potentially life threatening complications. Thrombolytic treatment, as well as reducing morbidity,¹ is known to reduce mortality in patients with acute myocardial infarction by approximately 25%.²⁻⁵ The benefit might be even greater in patients with concomitant severe cardiac failure.¹² These benefits would seem to outweigh the potential complications of inducing a fibrinolytic state in a patient with central venous cannulation. A significant number of myocardial reinfarctions requiring a repeated dose of thrombolytic agent occurred in the first few days after the initial infarction.⁸ Some of these patients would have had recent central venous cannulation. It seems important not to deny these patients further thrombolysis as their mortality would be particularly high.

This study, however, does demonstrate possible serious complications associated with central venous cannulation and thrombolytic

treatment. Two patients with minor haemorrhagic complications required blood or fresh frozen plasma transfusion, and blood loss may have been a factor responsible for hypotension in patient A. Physicians are traditionally trained to achieve central venous access via the subclavian vein. In view of the potential hazard associated with this practice, especially in the era of thrombolysis, it would seem prudent for physicians to be acquainted with central cannulation via a more compressible and visible route such as the femoral, brachial, or jugular vein.

Our results suggest that thrombolytic treatment in patients with central venous cannulation is associated with a low incidence of important bleeding complications. We conclude that similar to cardiopulmonary resuscitation,^{13,14} central venous cannulation is not a clear contraindication to thrombolytic treatment. It would seem prudent, however, to use the femoral, jugular, or brachial veins^{15,16} for cannulation of patients undergoing thrombolysis provided that appropriate training in the use of these routes is undertaken.

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